Lapatinib (L) is an oral receptor tyrosine kinase inhibitor which is used for the treatment of metastatic breast cancer. Adjuvant usage of L is being investigated in clinical phase III trials. There is no data regarding the side effects of combination of RT and L which may be a problem when L is used in the adjuvant setting. Lung is the most radiosensitive organ to observe late effects of RT. We evaluated if concurrent administration of L has any impact on the development of radiation induced pulmonary fibrosis in rats (RIPF).

Fourty female Wistar-albino rats (WAR) were divided into 4 experimental groups (G). G1 (control) did not receive any treatment, G2 (RT) received RT to whole thoracic region, G3 (L) received L without RT, G4 (L+RT) received L with RT. A total dose of 30 Gy in 10 fractions was given to both lungs with an anterior field at 2 cm depth. L equivalent to 1500 mg/day, 60 kg adult dose, were calculated according to the mean weight of rats, orally administrated with a feeding tube twice daily including the weekends until WAR were sacrificed. WAR were anesthetized and sacrificed 16 weeks after RT which was shown to be a sufficient period for the development of RIPF in rats. Paraffin sections (5 µm thick) of lungs were stained with hematoxylin-eosin and Masson's trichrome. A semiquantitative comparative analysis was performed among 4 groups by scoring the pulmonary injury between 0 and 4 according to the infiltration of inflammatory cells into the alveolar spaces, alveolar wall thickening and architectural deformation across the entire lung section. Each criterion had a possible score of 0 to 4, where 0 no injury; 1 minimal injury, 2 mild injury, 3 moderate injury, and 4 marked injury. The total lung injury score was calculated by summing the scores of these three parameters. Statistical analysis was performed.

Control group demonstrated normal pulmonary architecture. Lungs of the rats which received RT (G2) revealed inflammatory cell infiltration and increased amount of collagen fibers in the interstitial area leading to fibrosis, which thereby result in thickening of the alveolar septa and shrinkage of the size of the alveoli. RT damaged the lung architecture and G2 had a significantly lower lung histological injury score than did G1 (p<0.05). G3 showed minimal alveolar septal thickening and infiltration of inflammatory cells into the alveolar spaces which were not significantly different than G1. The histopathological findings in the group which L treatment was given together with RT (G4) was similar to those in G2 and was statistically significantly different compared to both the control group and G3 (p<0.05) (Figure 1).

This study shows that addition of Lapatinib to RT does not increase radiation induced pulmonary fibrosis in rats.
Fig. 1: Representative photomicrographs. A,B; thin alveolar walls. C,D; areas of intensive fibrosis and thickened alveolar walls. E; lapatinib alone had no adverse effect on the tissue structure. F; lapatinib+RT did not worsen the effects of RT on lung.